REMARKS

In a Final Office Action dated June 20, 2010, the Examiner withdrew the previous rejections of Claims 10, 42-44 and 69-70 under 35 U.S.C. §112, first paragraph, and correctly stated the status of the claims: Claims 10, 42-44, 47-49, 69 and 70 are currently under examination. The Examiner maintained the pending rejections of Claims 10, 42-44, 47-49, and 69-70 under 35 U.S.C. § 101 for allegedly lacking utility. Applicants respond to each of the Examiner's rejections below. In view of the remarks below, Applicants respectfully request reconsideration of the merits of this application.

REJECTIONS UNDER 35 U.S.C. § 101

Claims 10 and 42-44 are rejected as allegedly lacking either a specific and substantial-asserted utility or a well-established utility. The Examiner acknowledges that the specification discloses a utility for a polypeptide comprising mouse synaptogmin II BoNT/B binding domain and a utility for the ligand (*i.e.*, BoNT/B). However, the Examiner alleges that the specification does not provide utility for "a complex of a ligand and a polypeptide, wherein the ligand is BoNT/B" (see p. 3, Office Action). The Examiner asserts:

> *"the claims are [a] complex, that is all ready bound...screening assays that are used to identify compounds that bind or block binding are obtained by measuring the formation of a complex or the lack thereof. Thus, this invention cannot be used to screen or identify agents because the ligand and the polypeptide are bound. What is being measured? The complex is already formed. How can you screen for other agents?"* (page 4-5, detailed action).

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully submit that the lack of utility rejection should be withdrawn because contrary to the Examiner's assertion, the presently claimed invention provides a "specific and substantial-asserted utility or a well-established utility" as recognized by one of skill in the art. It is well settled law that a lack of utility rejection cannot be rendered "unless it has reason to doubt the objective truth of the statements contained in the written

description." *In re Cortright*, 165 F.3d 1353, 1356-1357 (Fed. Cir. 1999). See also *Brana*, 51 F.3d at 1566, 34 U.S.P.Q.2D (BNA) at 1441 ("The PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.") Lack of utility rejections are proper only where an applicant fails to identify any specific and substantial utility for the invention or fails to disclose enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention. *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966); *In re Fisher*, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005); *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), or where an assertion of specific and substantial utility for the invention made by an applicant is not credible.

In the present case, Applicants have clearly provided specific and substantial utility for the presently claimed invention. Specifically, the complex of claims 10 and 42-43 can be used in, for example, methods of identifying agents that can block the binding between BoNT/B and synaptogmin I or II, methods of identifying agents that can bind to the BoNT/B binding domain of synaptogmin I or II, and more. (See the Abstract and paragraphs [0045]-[0054] of the published application). These passages described a clear and specific utility of the complex of the present claims, as they particularly point to the BoNT/B binding domains of synaptogmin I or II and the binding of BoNT/B to those domains in the context of identifying agents that can block interaction between BoNT/B and synaptogmin I or II. Likewise, the utility of the presently claimed invention is substantial as defined in MPEP 2107.01 I.B. ("...Thus a "substantial utility" defines a "real world" use…") as identification of agents that can block binding between BoNT/B and synaptogmin I or II (see paragraph [0044]) has a "real world" use as is also evident from paragraph [0022] of the published application. The claimed sequences are clearly within the above scope and utility should not be denied based on lack of specific and substantial utility.

Further, in the context of the discussion in the background at paragraphs [0006]-[0008], one of ordinary skill in the art could not reasonably doubt the utility of the claimed subject matter, nor has the Examiner provided any evidence to that effect. For instance, enzyme/ligand complexes are well known in the art as useful in the investigation of compounds that would interfere with enzyme binding. Clearly, those familiar with the technological field of the invention will immediately recognize the utility of the presently claimed invention.

Specifically, it appears from the Office Action that the Examiner has not considered the numerous assays wherein alternative molecules (*e.g.*, toxins, random peptides, small molecules) are screened for their ability to outcompete the "*all* ready bound" ligand portion of a ligand complex for a position in the complex. It is well-established in the art that enzyme/ligand complexes are useful for investigating additional binding compounds or compounds that interfere with enzyme binding. In assays such as these, the compounds that are positive for binding/binding interference bind to the receptor of interest more strongly than the compound "*all* ready bound" to the receptor in complex. The binding/inhibitory compound replaces the ligand in the "*all* ready bound" complex. In short, those familiar with the technological field of the invention would immediately recognize the utility of the claimed complex.

Further, the Examiner has failed to recognize that the claimed complex is not static; the components of the complex are not irreversibly bound, rather, the complex can be used in an assay where one member of the complex is replaced (*e.g.*, outcompeted) by a compound being screened. Skilled artisans are familiar with numerous assays that utilize ligand complexes to measure toxin binding. Two such assays well known in the art are described below.

A standard *in vitro* assay might involve adding a fluorescent label to the ligand portion of the claimed complex, attaching the ligand-peptide complex to a solid surface (*e.g.*, a chip, assay well, *etc.*), and then measuring fluorescence to determine a baseline of 100% complex formation. A skilled artisan could then determine how much toxin is present in a given sample by adding said sample to the well/chip comprising the labeled complex, and allowing the toxin (if present in the sample) to compete for complex formation with the fluorescently labeled ligand-receptor complex. A skilled artisan understands that free fluorescence in/on the well/chip would indicate labeled toxin that is no longer bound in the complex. Alternatively, the skilled artisan could wash the well/chip, measure fluorescence, and determine that any decrease in fluorescence on the surface of the well/chip is due to non-labeled toxin present in the complex. A skilled artisan could carry out the aforementioned assay using the claimed complex without undue experimentation.

Fluorescence Resonance Energy Transfer (FRET) assays can utilize ligand complexes to measure binding or binding inhibition. In a FRET assay, both parts of the claimed complex (*i.e.* the polypeptide/receptor and the ligand) would be tagged with fluorescence labels that can undergo FRET which each other. When the complex forms, the fluorescence emission of the first label excites the second label leading to emission of fluorescence from the second label.

The tagged claimed complex could then be used to screen for compounds that inhibit complex formation (*i.e.*, the screened compound outcompetes the ligand portion of the complex for binding with the receptor/polypeptide portion of the claimed complex). To measure inhibition of complex formation, a skilled artisan would measure fluorescence; if the screened compound inhibited complex formation, the first label would be excited and emit fluorescence, but the second label would not be excited because the two labels would be too far apart to transfer energy. FRET assays are relatively simple and amenable to high throughput. A skilled artisan could readily carry out a FRET assay using the claimed complexes after reviewing the instant specification without undue experimentation.

Accordingly, Applicants submit that the invention recited in claims 10 and 42-44 clearly provides a specific and substantial utility, including"...methods of identifying agents that can block the binding between BoNT/B and synaptogmin I or II, methods of identifying agents that can bind to the BoNT/B binding domain of synaptogmin I or II..." (Abstract). Withdrawal of this rejection is requested.

Claims 47-49 and 69-70 stand rejected under 35 U.S.C. §101 for allegedly lacking utility, for the same reasons as set forth above. Claims 47 and 69 specify that the claimed ligand is an antibody that binds to the polypeptide portion of the complex. The arguments provided above for Claims 10, and 42-44 apply equally to the §101 rejection of claims 47-49 and 69-70. The claimed complex has utility in numerous assays, including those that are used to identify compounds that bind or block binding are obtained by measuring the formation of a complex or the lack thereof. The fact that the claimed complex is "*all* ready bound" does not prohibit measurement of further complex formation or lack thereof as the Examiner suggested. The fact that the ligand recited in the complexes of Claims 47 and 49 is an antibody does not alter the utility of the complex as described above.

Claims 47-49 also specify that the complex is located *in vivo* in a mammal. The Examiner alleged that the specification does not suggest any specific property or activity for the animals such that a utility would be well established for the animals (see p. 6 office action). Applicants disagree.

Figure 7B of the instant application shows protection of mice from BoNT/B toxicity using fragments of syt II. Syt II fragments were pre-mixed with gangliosides and BoNT/B for 10

minutes and then injected intravenously into mice. In these *in vivo* experiments, the mixture of syt II fragments, gangliosides and BoNT/B helps to protect mice from BoNT toxicity. From this experiment, a skilled artisan would understand that a complex containing the claimed polypeptide and an antibody that binds to that polypeptide, would be useful for reducing binding of BoNT/B to the polypeptide when the complex is located in vivo in a mammal. As argued previously, skilled artisans are well aware of methods for injecting or otherwise treating mammals with antibodies. Those skilled in the art are also aware of methods for treating animals with antibody complexes such as the complex claimed.

In the present case, Applicants have clearly provided specific and substantial utility for Claims 10, 42-44, 47-49, 69 and 70 as summarized in the abstract ("...methods of identifying agents that can block the binding between BoNT/B and synaptogmin I or II, methods of identifying agents that can bind to the BoNT/B binding domain of synaptogmin I or II..."), and in greater detail at paragraphs [0045]-[0054]. These passages are specific as they particularly point to the BoNT/B binding domains of synaptogmin I or II and the binding of BoNT/B to those domains in the context of identifying agents that can block interaction between BoNT/B and synaptogmin I or II. Likewise, the utility is substantial as defined in MPEP 2107.01 I.B. ("...Thus a "substantial utility" defines a "real world" use…") as identification of agents that can block binding between BoNT/B and synaptogmin I or II (see paragraph [0044]) has a "real world" use as is also evident from paragraph [0022]. The claimed complexes are clearly within the above scope and utility should not be denied based on lack of specific and substantial utility.

Accordingly, Applicants respectfully submit this rejection should be withdrawn.

SUMMARY AND FEES

In the present response Applicants present argument against the Examiner's rejections. Reconsideration of the application and allowance are respectfully requested in view of the arguments presented above. If all the claims are not allowed, Applicants request a telephone interview with the Examiner and his supervisor.

Applicants have enclosed a Request for Continued Examination and a Petition for Two Months Extension of Time. The Commissioner is authorized to charge any fees under 37 CFR § 1.17 that may be due in this application to Deposit Account 17-0055. If further fees are necessary, please charge Deposit Account 17-0055. The Commissioner is also authorized to treat this paper and any future reply in this matter requiring a petition for an extension of time as incorporating a petition for extension of time for the appropriate length of time as provided by 37 CFR § 136(a)(3).

Respectfully submitted,

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